

BIOGRAPHICAL SKETCH

NAME: Mahamaya Biswal

eRA COMMONS USER NAME (credential, e.g., agency login): MAHAMAYA

POSITION TITLE: Postdoctoral researcher at Department of Molecular and Cellular Physiology

EDUCATION/TRAINING:

| INSTITUTION AND LOCATION | DEGREE | Completion Date MM/YYYY | FIELD OF STUDY |
|--|---------------------------------|----------------------------|---------------------------------------|
| D.Y Patil University, MH,India | B.Tech- M.tech integrated | 06/2013 | Biochemistry |
| University of California Riverside, CA,USA | PhD | 06/2022 | Biochemistry and Molecular Biology |
| University of California Riverside, CA,USA | Postdoctorate | 07/2023 | Biochemistry and Molecular Biology |
| Stanford University, Palo Alto, CA, USA | Postdoctorate | Present | Molecular and Cellular Biology |

A. Personal Statement

From an early age, I was captivated by biology and the molecular mechanisms that govern life, which inspired me to pursue an academic career in science. My journey began with a biotechnology degree at D.Y. Patil University, where I developed a strong interest in biochemistry. During my master's, I conducted research at BARC, Mumbai, investigating the role of cAMP receptor protein in persister cell formation, followed by a research internship at ACTREC, where I characterized breast cancer-related proteins ZBRK1 and BRCA1.

After three years in the biotech industry in Mumbai, honing my skills in protein biochemistry and purification, I joined the Ph.D. program at UC Riverside. My doctoral research in Dr. Jikui Song's lab focused on the structural biology of SARS-CoV-2 viral proteins. I successfully completed a project investigating the NSP7-8 complex, a cofactor essential for the viral RNA polymerase NSP12, solving its X-ray crystal structure and performing biophysical characterization to study its dynamic association with NSP12 (*Nucleic Acids Research*, 2021). I also initiated and completed a project characterizing the structural basis of complex formation between the SARS-CoV-2 nucleocapsid protein and the human stress granule protein G3BP1, narrowing down the interaction sites and solving the structure of the complex at 2.5 Å resolution (*Journal of Molecular Biology*, 2022). Additionally, I contributed to a collaborative project on the structural basis for STAT2 antagonization by DENV2 NS5, published in *Communications Biology* (2024). Throughout my Ph.D., I supervised new graduate and undergraduate students, further developing my mentoring and leadership skills.

Motivated to bridge basic science and therapeutic discovery, I joined Dr. Georgios Skiniotis's lab at Stanford to gain expertise in GPCR structural biology. When Dr. Skiniotis relocated, I decided to join Dr. Tino Pleiner's lab, being particularly impressed by his outstanding cell biology expertise, mentorship skills, and the innovative research on membrane protein biogenesis conducted in his group. I was especially curious about the role of insertase in ensuring proper folding of membrane proteins, and Tino's pioneering use of nanobody technologies to dissect these processes offered an exciting opportunity to dive deeper into the biogenesis and quality control of membrane proteins. In Dr. Pleiner's lab, I now investigate membrane protein quality control at the ER membrane using advanced cryo-EM and biochemical approaches, focusing on the assembly and maturation of voltage-gated ion channels and the development of nanobodies for structural and functional studies.

Looking ahead, my career goal is to lead an innovative research program in biotechnology, translating structural discoveries into therapeutic solutions for neurological disorders. I am committed to fostering inclusivity and advancing women in science, as demonstrated by my active membership in AWIS, BioAIMS, and BSS (India). I have mentored female scientists at various academic stages, supported women graduate students through stressful periods, helped international students find the right labs, and encouraged young women scientists to persevere through academic challenges. By uplifting and mentoring these individuals, I have contributed to a more equitable and supportive research environment.

The Shoshana Levy Fellowship will be pivotal for my scientific independence and my goal of leading a structural biology research program focused on membrane protein misfolding diseases. This support will enable me to advance my research, deepen my expertise in cryo-EM, and develop the mentorship and leadership skills necessary to establish an impactful academic career.

Publications that highlight my experience and qualifications for this project:

- 1) Beyond Stress Granules: G3BP1 and G3BP2 Redundantly suppresses SARS CoV-2 infection; Duo Xu, M Biswal, Quan-Qing Zhang, Chenjin Ye, Luis Martinez-Sobrido, Jikui Song, Rong Hai (Under Review, Journal-Viruses)
- 2) A conformational selection mechanism of flavivirus NS5 for species-specific STAT2 inhibition; M Biswal, W Yao, J Lu, J Chen, R Hai, J Song, Communications biology, 2024.
- 3) Two conserved oligomer interfaces of NSP7 and NSP8 underpin the dynamic assembly of SARS-CoV-2 RdRP; M Biswal, S Diggs, D Xu, N Khudaverdyan, J Lu, J Fang, G Blaha, R Hai, J Song, Nucleic Acids Research, 2021
- 4) SARS-CoV-2 Nucleocapsid Protein Targets a Conserved Surface Groove of the NTF2-like Domain of G3BP1; M Biswal, J Lu, J Song, Journal of Molecular Biology, 2022
- 5) Substrate deformation regulates DRM2-mediated DNA methylation in plants; J Fang, SM Leichter, J Jiang, M Biswal, J Lu, ZM Zhang, W Ren, J Zhai, Science Advances 7 (23), eabd9224
- 6) Complex DNA sequence readout mechanisms of the DNMT3B DNA methyltransferase, M Dukatz, S Adam, M Biswal, J Song, P Bashtrykov, A Jeltsch, Nucleic acids research 48 (20), 11495-11509
- 7) Review Devil's tools: SARS-CoV-2 antagonists against innate immunity, D Xu, M Biswal, A Neal, R Hai, Current research in virological science; Volume 2, 2021, 100013
- 8) Mechanistic basis for maintenance of CHG DNA methylation in plants
J Fang, J Jiang, SM Leichter, J Liu, M Biswal, N Khudaverdyan, X Zhong, J Song. Nature Communications 13 (1), 1-12
- 9) Structure of DNMT3B homo-oligomer reveals vulnerability to impairment by ICF mutations; L Gao, Y Guo, M Biswal, J Lu, J Yin, J Fang, X Chen, Z Shao, M Huang, Y Wang, G Wang, J Song; Nature Communications 13 (1), 1-11
- 10) Structural basis to characterize transactivation domain of BRCA1, LR Yadav, MN Biswal, MV Hosur, NSKumar, AK Varma, Journal of Biomolecular Structure and Dynamics 35 (1), 1-7
- 11) Tetrameric ZBRK1 DNA binding domain has affinity towards cognate DNA in absence of zinc ions, LR Yadav, MN Biswal, MV Hosur, AK Varma, Biochemical and biophysical research communications 450(1), 283-28

B. Positions and Honors

Positions and Employment

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|---------------|---|
| 2024- Present | Postdoctoral researcher, Department of Molecular and Cellular Physiology, Stanford University, Stanford, CA, USA Postdoc faculty Sponsor: Dr. Tino Pleiner |
| 2023 – 2024 | Postdoctoral researcher, Department of Molecular and Cellular Physiology, Stanford University, Stanford, CA, USA Postdoc faculty Sponsor: Dr. Georgios Skiniotis |
| 2012 – 2023 | Postdoctoral fellow, University of California Riverside, CA, USA Advisor: Dr. Jikui Song |
| 2017-2022 | Graduate student, University of California Riverside, CA, USA Advisor: Dr. Jikui Song |

Professional Memberships

2025 – Present Member, Maternal and Child Health (MCHRI)

Honors

2022 HEERF Dissertation Year (DYP) fellowship

2021 – 2022 Wedding prize awarded during Wedding Symposium at University of California Riverside, CA, USA

2018 – 2019 Best Poster presentation at wedding Symposium at University of California Riverside, CA, USA

B. Contributions to Science

1. Structural insights into SARS CoV-2 viral proteins

During my PhD, I focused on understanding the structural basis of key SARS-CoV-2 proteins involved in viral replication and host immune evasion. I solved the X-ray crystal structure of the NSP 7-8 complex, a critical cofactor for the NSP12 RNA Polymerase, providing fundamental insights into the assembly of the viral replication machinery. This work helped inform potential antiviral strategies targeting polymerase function. Additionally, I characterized the interaction between the nucleocapsid protein and the host stress granule protein G3BP1, which the virus hijacks to evade immune responses. By mapping the interaction sites and determining the structure of the N-protein peptide (1-25) in complex with G3BP1 NTF2, my work contributed to understanding how SARS-CoV-2 disrupts host cellular defense mechanisms.

Relevant Publications:

- a. Biswal M, Diggs S, Xu D, Khudaverdyan N, Lu J, Fang J, Blaha G, Hai R, Song J, Two conserved oligomer interfaces of NSP7 and NSP8 underpin the dynamic assembly of SARS-CoV-2 RdRP, *Nucleic acids research* 49 (10), 5956-59661.
- b. Biswal M, Lu J, Song J, SARS-CoV-2 Nucleocapsid Protein Targets a Conserved Surface Groove of the NTF2-like Domain of G3BP1, *Journal of molecular biology* 434 (9), 167516

2. Mechanistic insights into DENV2 immune invasion: DENV2 NS5-STAT2 interaction

I investigated the interaction between DENV2 NS5 and STAT2 protein in the host, a critical mechanism by which the virus suppresses the host interferon response and evades immune detection. Through biochemical and structural studies, I characterized how NS5 mediates STAT2 degradation, thereby disrupting antiviral signaling pathways and promoting viral replication. These findings provide crucial insights into DENV2 pathogenesis and have significant implications for the development of targeted antiviral strategies aimed at restoring host immune defenses.

Relevant Publications:

- a. Biswal M, Yao W, Lu J, Chen J, Morrison J, Hai R, Song J, A conformational selection mechanism of flavivirus NS5 for species-specific STAT2 inhibition, *Communications Biology* 7 (1), 76

3. Contributions to epigenetics and Gene regulation studies

Beyond Virology, my research in epigenetics has significantly contributed to the field of chromatin remodeling and histone modifications, which are fundamental mechanisms of gene regulation. My collaborative efforts led to structural characterization studies on DNA methylation regulators, including the DRM2-mediated DNA methylation pathway in plants and the DNMT3B DNA methyltransferase

complex in humans, which elucidated how complex DNA sequence readout mechanisms regulate methylation patterns.

Relevant Publications:

- a. Dukatz M, Adam S, Biswal M, Song J, Bashtrykov P, Jeltsch A, Complex DNA sequence readout mechanisms of the DNMT3B DNA methyltransferase, *Nucleic acids research* 48 (20), 11495-11509
- b. Fang J, Leichter SM, Jiang J, Biswal M, Lu J, Zhang Z, Ren W, Zhai J, Cui Q, Zhong X, Song J, Substrate deformation regulates DRM2-mediated DNA methylation in plants, *Advances* 7 (23), eabd9224

4. Biophysical characterization of Breast cancer associated proteins

I have conducted biophysical and biochemical characterization of ZBRK1 and BRCA1, two proteins crucial to breast cancer progression and DNA damage repair. My research provided insights into their structural and functional roles, contributing to a better understanding of tumor suppression mechanisms and potential therapeutic interventions.

Relevant Publications:

- a. Yadav LR, Biswal M, Hosur MV, Varma AK, Tetrameric ZBRK1 DNA binding domain has affinity towards cognate DNA in absence of zinc ions, *Biochemical and biophysical research communications* 450 (1), 283-288
- b. Yadav LR, Biswal M, Hosur MV, Kumar NS, Varma AK, Structural basis to characterize transactivation domain of BRCA1, *Journal of Biomolecular Structure and Dynamics* 35 (1), 1-7

Complete List of Published Work in My Bibliography:

<https://pubmed.ncbi.nlm.nih.gov/collections/65531705/?sort=pubdate>